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REMARKS

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Claims 45-82 are in this application.

According to the page 2 of the Office Action, claims 45-82 are rejected under 35 USC 103(a) as being unpatentable over Ishikawa et al. (US Patent no. 4,522,879) and de Souza et al. (US Patent No. 6,514,986) in view of Ishibashi et al. (US Patent 6,638,534) or Rubinfeld et al. (US Patent No. 5,824,668). This is respectfully traversed.

Independent claim 45 of this application defines a stable pharmaceutical composition that defines the composition as a solution that "is a substantially isotonic aqueous solution at a physiologically compatible pH." This claim also provides that "the concentration of the drug that is maintained in solution with the solubilizing agent is above the practical limit of solubility of the drug as compared to the solubility of the drug when the drug is not in solution with the solubilizing agent."

Ishikawa et. al. (US patent No. 4,522,879) discloses racemic benzoheterocyclic compounds and the composition comprising the racemic compounds, the injectable compositions of the '879 patent, preparation example 1, column 52, lines 45-60 discloses use of sodium salt of racemic 9-fluoro-8-(4-hydroxy-1-piperidinyl)-5-methyl-6,7-dihydro-1-oxo-1H,5H-benzo[i,j]quinolize-2-carboxylic acid, and glucose in distilled water. However, the use of sodium salt causes severe phlebitis, therefore such a composition cannot be used.

De Souza et. al. (US patent No. 6,514,986) claims polymorphs of arginine salt of S-(-)-9-fluoro-8-(4-hydroxy-1-piperidinyl)-5-methyl-6,7-dihydro-1-oxo-1H,5H-benzo[i,j]quinolize-2-carboxylic acid, method of treating disease caused by microbial infection and formulation comprising the polymorph. The formulation claims 29 and 30 of '986 patent define the forms as a tablet, coated tablet, coated tablet core, capsule, patch, powder, pellet, granule and hard gelatin capsule. The '986 patent does not disclose any pharmaceutical composition of arginine salt of S-(-)-9-fluoro-8-(4-hydroxy-1-piperidinyl)-5-methyl-6,7-dihydro-1-oxo-1H,5H-benzo[i,j]quinolize

-2-carboxylic acid, as a solution, using a solubilizing agent.

The problem that Ishibashi et. al. (US patent No. 6,638,534) addresses is the formulation of solid compositions such that the drug is released in the intestine rather than elsewhere in the digestive tract. According to column 2, lines 38-49, Ishibashi seeks to solve this problem by "a preparation in which a core material containing a medicinal substance coated with a mixed film of hydrophobic organic compound-enteric polymer, has a unique releasing behavior in that the preparation releases no medicinal substance in an acidic solution but releases a medicinal substance quickly in a neutral or basic solution after a certain period of time (lag-time). The inventors have also found that the lag-time can be controlled by changing the coating amount of film and the ratio of the amount of the hydrophobic organic compound to the amount of the enteric polymer."

The disclosure of solubilizing agents cyclodextrin and arginine column 11, lines 31-34 is mentioned as one of the additives for a solid composition to be released at a selected location in the intestine. It is specifically stated at column 11, lines 6-8, that "all additives can be employed suitably as long as the additives can be employed for a solid preparation." The '534 patent does not disclose any information pertaining to the formation of a solution and maintaining the concentration of a drug in solution.

Following the US Supreme Court's decision in **KSR v. Teleflex** (Docket US No. 04-1350 April 30, 2007), it is clear that one of ordinary skill in the art would not have considered Rubinfeld et al. (US Patent No. 5,824,668) because a person of ordinary skill, based on the disclosure of Rubinfeld would not be able to predict that cyclodextrins could be used in the formulation of solutions of the compounds included in claim 45.

Furthermore, the Examiner is relying on impermissible hindsight.

According to MPEP 2141 when applying 35 USC 103, the following tenets of patent law must be adhered to:

(A) The claimed invention must be considered as a whole; (B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination; (C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention and (D) reasonable expectation of success is the standard with which obviousness is determined.

A reference must be considered for what it would teach someone skilled in the art at the time the invention was made and not be applied based on "hindsight". See **Panduit Corp. v. Dennison Manufacturing Co.**, 227 USPQ 337, 343 (Fed. Cir. 1985):

It is impermissible to first ascertain factually what applicants did and then view the prior art in such a manner as to select from the random facts of that art only those which may be modified and then utilized to reconstruct appellants' invention from such prior art.

In making its obviousness determination, a court must view the prior art without reading into that art the patent's teachings. **Vandenberg v. Dairy Equipment**, 224 U.S.P.Q. 195 (Fed. Cir. 1987) citing **In re Sponnoble**, 160 U.S.P.Q. 237 (CCPA 1969). In **Uniroyal . Rudkin-Wiley**, 50 U.S.P.Q.2d 1434, 1438 (Fed. Cir. 1988) the CAFC stated:

The obviousness standard, while easy to expound, is sometimes difficult to apply. It requires the decision maker to return to the time the invention was made. The invention must be viewed not with the blueprint drawn by the inventor, but in the state of the art that existed at the time...That which may be clear and thus obvious to a court, with the invention fully diagramed and aided by experts in the field, may have been a breakthrough of substantial dimension when first unveiled [citations omitted]. In this case we are convinced that the district court misapplied the obviousness standard. It has impermissibly used hindsight to reconstruct the claimed invention

from prior art with the invention before it and aided by Uniroyal's expert, rather than viewing the invention from the position of a person of ordinary skill at the time it was made. When prior art references require selective combination by the court to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight gleaned from the invention itself.

The Examiner has not established that at the time the invention claimed in this application was made that one skilled in the art would have first, considered these references and second, would have combined references that disclose information about solid formulations and structurally unrelated drugs for different purposes (e.g. Rubinfeld) to prepare a composition that is a solution.

Therefore, for the reasons explained above, it is respectfully requested that this rejection be withdrawn.

According to the Office Action:

- 1) claims 45-82, are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12, 1, 18, 29 and 30 of U.S. Patent No. 6,514,986 in view of Ishibashi, et al. (U.S. Patent 6,638,532) or Rubinfeld, et al. (U.S. Patent No. 5,824,668).
- 2) Claims 45-82 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,608,078 in view of Ishibashi, et al. (U.S. Patent No. 6,638,534) or Rubinfeld, et al. (U.S. Patent No. 5,824,668).
- 3) Claims 45-82 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 and 8-111 of U.S. Patent No. 6,664,267 in view of Ishibashi, et al. (U.S. Patent 6,638,534) or Rubinfeld, et al. (U.S. Patent No. 5,824,668).
- 4) Claims 45-82 are rejected on the ground of nonstatutory obviousness-type double

patenting as being unpatentable over claims 1-10 of U.S. Patent 6,750,224 in view of Ishibashi, et al. (U.S. Patent No. 6,638,534) or Rubinfeld, et al. (U.S. Patent No. 5,824,668) and

5) Claims 45-82 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 6, 7, 21-23, 29-38 and 45-47 of copending Application No. 09/566,875 in view of Ishibashi, et al. (U.S. Patent No. 6,638,534).

Applicants will address the nonstatutory obviousness-type double patenting rejections at the time the Examiner indicates that one or more of the claims are allowable.

In view of the cancellation of claim 67 and the amendments of claims 45, 68, 69 and 81, it is respectfully requested that the rejection under 35 USC 112, first paragraph be withdrawn.

It is submitted that the present application is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted,



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